



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

DECLARATION OF:

Roberts et al.

SERIAL NO.: 08/304,147

FILING DATE: 9/12/94

RE: Method and Compositions To
Assess Oxidative Stress
In Vivo

GROUP ART UNIT

EXAMINER

The Honorable Commissioner of
Patent and Trademark
Washington, D.C. 20231

Sir:

132 DECLARATION

I, Lawrence J. Marnett, declare:

1. I received my B.S. degree from Rockhurst College in 1969, and my Ph.D from Duke University in 1973. I am currently the Mary Geddes Stahlman Professor of Cancer Research, Professor of Biochemistry, and Professor of Chemistry at Vanderbilt University. I am Director of the A.B. Hancock, Jr. Memorial Laboratory for Cancer Research and Research Director of The Vanderbilt Cancer Center. I have been a member of the editorial boards of nine scientific journals including the Free Radical Biology and Medicine (1985-1994). I am currently Editor-in-Chief of Chemical Research in Toxicology. I have been actively involved in research in the areas of prostaglandins and free radicals for over 20 years. My curriculum vitae is attached hereto as Exhibit A.

2. I have reviewed the above-captioned application and Morrow et al., "Noncyclooxygenase Oxidative Formation of a Series of Novel Prostaglandins: Analytical Ramifications for Measurement of Eicosanoids," Anal. Biochem. 184:1-10 (1990).

3. The above application discloses that a series of prostaglandin F₂-like compounds, now referred to as isoprostanes, are produced in vivo by a free radical catalyzed process. The application also discloses that these prostaglandin F₂-like compounds can be detected in normal human biological fluids and that their formation increases dramatically in settings of oxidant stress in vivo. The application claims methods for assessing oxidative stress in vivo by quantification of these prostaglandin F₂-like compounds.

4. The discovery by the Applicants that prostaglandin F₂-like compounds were produced *in vivo* was surprising because it demonstrated that compounds related to prostaglandins could be formed chemically instead of enzymatically.

5. Prior to the Applicants' discovery there was no convincing evidence that free radical-catalyzed peroxidation of lipids actually occurred *in vivo*. This was hotly debated and the balance of opinion was that if peroxidation did occur *in vivo* it could only be demonstrated in animal models treated with extremely toxic agents designed to trigger oxidative stress. However, Applicants demonstrated that this process occurs in normal human beings not treated with unusual or toxic agents. Furthermore, Applicants showed that lipid peroxidation increases in human beings in some clinical and lifestyle conditions (e.g.

smoking). Additionally, Applicants demonstrated the ability to discriminate renal production of isoprostanes from systemic production of isoprostanes and to detect the production of isoprostanes in individual tissues. Roberts et al. provided the first convincing evidence that peroxidation occurred *in vivo*. Their findings were stunning to the scientific community, even to experts in the field of oxidative stress.

I hereby declare that all statements made herein are believed to be true; and further, these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of this application or any patent issuing thereon.

Dated

11/23/94

Lawrence J. Marnett
Lawrence J. Marnett



CURRICULUM VITAE

Name Lawrence J. Marnett

Social Security 511-52-1113

Born Kansas City, Kansas - November 22, 1947

Citizenship USA

Marital Status: Married, Two children

Campus Address Department of Biochemistry
Vanderbilt University School of Medicine
Nashville, TN 37232
(615) 343-7329

Education B.S., Rockhurst College, *cum laude*, 1969
Ph.D., Duke University, 1973
Dissertation: *"The Thermal and Photochemical Decomposition of
Unsymmetric Azo Compounds"* Professor Ned A. Porter, Advisor

Professional Positions

Research Associate, Karolinska Institutet, in collaboration with Professor Bengt Samuelsson, 1973-1974

Research Associate, Wayne State University, in collaboration with Professor A. Paul Schaap, 1974-1975

Assistant Professor Chemistry, Wayne State University, 1975-1980; *Associate Professor of Chemistry*, Wayne State University, 1980-1983; *Professor of Chemistry*, Wayne State University, 1983-1989

Mary Geddes Stahlman Professor of Cancer Research, Professor of Biochemistry, Professor of Chemistry, Vanderbilt University School of Medicine, 1989-

Director, A.B. Hancock, Jr. Memorial Laboratory for Cancer Research, Vanderbilt University School of Medicine, 1989-

Associate Director for Basic Science, The Vanderbilt Cancer Center, 1993-

Awards and Honors

Probus Club Award for Academic Achievement (1980)
Wayne State University President's Award for Excellence in Teaching (1980)
American Cancer Society Faculty Research Award (1982)
Sigma Xi Research Award (1986)
Wayne State University Distinguished Graduate Faculty Award (1988)
Michigan Association of Governing Boards Distinguished Faculty Award (1988)
National Cancer Institute Outstanding Investigator Grant (1988-1995)

Scientific Societies

American Chemical Society
American Society of Biochemistry and Molecular Biology
American Association for the Advancement of Science
International Society for the Study of Xenobiotics
American Association for Cancer Research
Society of Toxicology
The Oxygen Society - Fellow

Honorary Societies

Alpha Sigma Nu
Phi Lambda Upsilon
Sigma Xi

Professional Activities

Member, Species Comparison in Carcinogenesis Study Section (ad hoc), National Institutes of Health, 1981.
Visiting Associate Professor of Biochemistry, University of Texas Health Science Center at Dallas, 1981.
Member, Chemical Pathology Study Section, National Institutes of Health, 1982-1985.
Organizer, Symposium on Arachidonic Acid Metabolism, American Chemical Society National Meeting, Chicago, Illinois, 1985.
Visiting Scholar, University of Toledo, Department of Chemistry, 1986.
Coorganizer, Symposium on Peroxidase Mechanisms in Chemical Carcinogenesis, Federation of American Societies for Experimental Biology. Annual Meeting, St. Louis, Missouri, 1986.
Organizing Committee, International Conference on Anticarcinogenesis and Radioprotection, Rockville, Maryland, 1987.
Organizing Committee, Gordon Conference on Oxygen Radicals in Biology and Medicine, Santa Barbara, California, 1987.
Member, Medical Biochemistry Study Section (ad hoc), National Institutes of Health, 1988.
Vice-Chairman, Gordon Conference on Oxygen Radicals in Biology and Medicine, Santa Barbara, California, 1989.
Organizing Committee, Eicosanoids and Bioactive Lipids in Cancer & Radiation Injury - 1st International Conference, Detroit, Michigan, 1989.
Chairman, Gordon Conference on Oxygen Radicals in Biology and Medicine, Santa Barbara, California, 1990.
International Advisory Committee, Seventh International Conference on Prostaglandins and Related Compounds, Florence, Italy, 1990.
International Scientific Advisory Committee, International Symposium on Biological Oxidation Systems, Bangalore, India, 1989.
Organizing Committee, Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury - 2nd International Conference, Berlin, West Germany, 1991.
Program Advisory Committee, Prostaglandins, Leukotrienes and Lipoxins, Washington, D.C., 1991.
International Advisory Committee, Montreal Conference on Prostaglandins and Related Compounds, Montreal, Canada, 1992.
Organizer, Symposium on Peroxidases and Peroxyl Radicals in Toxicity, Society of Toxicology Meeting, Seattle, Washington, 1992.

Program Committee, Thirteenth Enzyme Mechanism Meeting, Key Largo, Florida, 1993
Organizing Committee, Third International Meeting on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury - Washington, D.C. 1993
International Advisory Committee, 9th International Conference on Prostaglandins and Related Compounds, Florence, Italy, 1994
Coorganizer, American Cancer Society Workshop on NSAID's and Colon Cancer Prevention, Atlanta, Georgia, 1994
Coorganizer, Symposium on Arachidonic Acid Metabolism, Chemical Congress of Pacific Basin Societies, Honolulu, Hawaii, 1995

Editorial Activities

Member, Editorial Board, *The Journal of Biological Chemistry*, 1983-1987.
Member, Editorial Board, *Archives of Biochemistry and Biophysics*, 1984-1993
Member, Editorial Board, *Cancer Research*, 1985-1986.
Member, Editorial Board, *Free Radical Biology and Medicine*, 1985 -1994
Member, Editorial Board, *Carcinogenesis*, 1986-1988
Member, Editorial Board, *Advances in Pharmacology*, 1987-
Series Co-Editor, *Prostaglandins, Leukotrienes, and Cancer*, Martinus-Nijhoff Publisher, 1984-
Editor-in Chief, *Chemical Research in Toxicology*, 1987-
Member, Editorial Board, *Redox Reports*, 1994-1996

Graduate Degrees Directed

M.S.

Bienkowski, Michael, M.S., 1980
"Oxygen-18 Investigation of the Arachidonic Acid Dependent-Cooxygenation of Xenobiotics"
Prust, Robert M., M.S., 1981
"Test for the Intermediacy of 11-Hydroperoxy-Arachidonic Acid in Prostaglandin Biosynthesis"
Wilhelm, Jeffrey, M.S., 1986
"The Cooxidation of Nafazatrom by Prostaglandin H Synthase"
George, Alister, M.S., 1987
"A Method for In Situ Generation of Prostaglandin H₂"
Carolin, Kathryn, M.S., 1989
"Synthesis of Site-Specific 1,N2Ethenodeoxyguanosine in a Small Oligonucleotide"
Laudicina, D.C., 1989
"Synergistic Stimulation of Lipid Peroxidation by Organic Hydroperoxides and Ascorbate"

M.A.

DeSantis, Nancy, M.A., 1988

Ph.D.

Pagels, William R., Ph.D., 1981

"The Peroxidase Activity of Prostaglandin Endoperoxide Synthetase"

Reed, Gregory A., Ph.D., 1981

"Metabolism and Activation of Benzo[a]pyrene and Benzo-Ring Derivatives During Prostaglandin Biosynthesis"

Dix, Thomas, Ph.D., 1983

"The Mechanism of the Fatty Acid Hydroperoxide Dependent-Epoxidation of 7,8-Dihydroxy-7,8-Dihydrobenzo[a]pyrene"

Basu, Ashis, Ph.D., 1984

"Studies on the Mutagenicity of Malondialdehyde and Related Compounds"

Weller, Paul E., Ph. D., 1985

"Chemical and Enzymatic Transformations of 5-Phenyl-4-Pentenyl-1-Hydroperoxide"

Battista, John R., Ph.D., 1986

"The Role of Hydroperoxide-Dependent Oxidations in the Metabolic Activation of Chemical Carcinogens"

Bull, Arthur W., Ph.D., 1986

"Lipid Peroxidation and Intestinal Carcinogenesis: Structure-Activity Relationships and Analytical Methods"

Samokyszyn, Victor, M., Ph.D., 1987

"Oxidation of 13-Cis-Retinoic Acid by Iron-Oxo Intermediates of Prostaglandin H Synthase and Unsaturated Fatty Acid-Derived Peroxyl Radicals"

Labeque, Regine, Ph.D., 1988

"Reaction of Allylic Hydroperoxides With Metals and Metalloproteins"

Markey, Christine M., Ph.D., 1988

"Interaction of the Peroxidase and Cyclooxygenase Activities of Prostaglandin H Synthase: Characterization of the Peroxidase"

O'Hara, Shawn M., Ph. D., 1988

"Studies on the Reaction of β -Alkoxy-Acroleins With Guanine Nucleosides and Frameshift Mutagenesis in Salmonella typhimurium hisD3052"

Plé, Patrick, Ph.D., 1988

"Structure-Activity Studies of Alkyl Aryl Sulfides and Related Compounds as Reducing Substrates for the Peroxidase Activity of Prostaglandin H Synthase"

Chen, Ying Nan Pan, 1988

Studies on the Structure and Function of Prostaglandin H Synthase

Stone, Koni K., 1990

Studies of the Reaction of Malondialdehyde with Nucleosides

Reddy, Ashok, 1990

Separation of (+)-Syn and (-)-Anti-Benzo[a]pyrene Dihydrodiolepoxide-DNA Adducts in [32P]-Postlabeling Analysis: Application to the Study of Pathways of Benzo[a]pyrene Metabolism in Mouse Skin In Vivo

Odenwaller, Rebecca, 1991

Studies on the Role of the Peroxidase of Prostaglandin H Synthase in Its Cyclooxygenase Reaction"

Benamira, Mounir, 1992

Mutagenesis by Malondialdehyde. Random and Site-Specific Approaches to the Role of Individual DNA Adducts

Wells, Isabelle, 1992

Chemical Modification of Prostaglandin H Synthase by N-Acetylimidazole and Reactive Indomethacin Derivatives

Chapeau, Marie-Christine, 1992

Strategies for Construction of Carcinogen Adducts of Deoxynucleosides

Administrative Activities

Wayne State University

Chairman, Education Committee, American Chemical Society, Detroit Section, 1976-1977.

Alternate Councilor, American Chemical Society, 1978-1980.

Graduate Recruiting Officer, Department of Chemistry, 1980-1982.

Personnel Committee, Department of Chemistry, 1981-present.

Member, Chairman Search Committee, Biochemistry Department, Wayne State University School of Medicine, 1985.

External Program Review, Eppley Institute for Cancer Research, University of Nebraska, 1985.

Comprehensive Cancer Center of Metropolitan Detroit, Developmental Grants Review Board, 1984-present.

Member, Molecular Biology Center Advisory Committee, Wayne State University, 1985-1988.

Member, Dean Search Committee, College of Pharmacy and Allied Health, Wayne State University, 1987

University Grant Review Committee, Science Subcommittee, 1987

External Program Review, Toxicology Program, University of California San Francisco, 1987

Wayne State University Biomedical Research Committee, 1988

Nominating Committee, Society of Toxicology, Molecular Biology Specialty Section, 1988

Vanderbilt University

Cancer Center Advisory Committee, 1989-
Ernest Goodpasture Chair in Experimental Pathology Search Committee, 1990-
American Chemical Society, Nashville Section, Program Committee, 1990
Medical Oncology Division Chairman, Department of Medicine, Search Committee, 1990-1992
Pediatric Pulmonary Specialized Center of Research, Scientific Advisory Committee, 1990-
American Association of Cancer Research, "Minuteman" Scientific and Public Education Committee, 1990-
American Cancer Society Institutional Research Grant Committee, 1990-; Chairman, 1994-
School of Medicine, Institutional Self-Study, Research Committee, 1991
Biomedical Science Seminar Committee, 1991
Biochemistry Department Graduate Education Committee, 1991-
Chemistry Department Divisional Organization Committee, 1990
American Association for Cancer Research, G.H.A. Clowes Award Committee, 1991
American Association for Cancer Research, Publications Committee, 1991-1994
American Association for Cancer Research, Publications Committee, Chairman, 1994-1997
Biochemistry Department Committee on Curriculum Design, 1992
Clinical Pharmacology Center Executive Committee, 1992-
External Advisory Committee, Program Project in Sickle Cell Biology, University of Chicago, 1992-
Toxicology External Advisory Committee, University of Arizona, 1992-
Vanderbilt Cancer Center Advisory Board, 1993-
National Institute of Environmental Health Sciences Review Committee, 1993
Vanderbilt Cancer Center Research Programs Committee, Co-Chairman, 1994-
Vanderbilt Cancer Center Shared Resources Committee, Chairman, 1994-

Teaching

Wayne State University

Chem 100 Chemistry for Non-Science Majors
Chem 101 General Chemistry for Occupational Therapists
Chem 103 General Chemistry for Pre-Nursing Students
Chem 105 General Chemistry
Chem 560 Introductory Biochemistry
Chem 660 Advanced Biochemistry
Chem 878 Enzyme Mechanism
Chem 879 Chemical Carcinogenesis

Vanderbilt University

Bio 321 Basic and Advanced Biochemistry
Bio 336 Biochemical Toxicology and Carcinogenesis
Bio 337 Student Seminar
Bio 337 Molecular Aspects of Cancer Research
Bio 301 Molecular Structure and Function

Ph.D. Committees

Vanderbilt University

Christopher Smith
Anita Corbett
Megan Robinson
Stephanie Dew
Michael McCarthy
Christopher Smith
Kevin Raney
Liang Zhou
Seong Jin Kim
Karen Richards
Kristin Johnson
Laura Neidernhofer
Sandra Miller-Davis
Bin-Bin Fang
Jason Weisenseel
S. Krisnaswamy
David Johnston
Gary Latham
Cheryl Lanzo
Stephen Fink
Merilyn Blair
Kathy Wheeler
Sin Han
Eleanor McCarthy
David Ferguson

Consulting Activities

Searle and Co., 1981
Warner-Lambert/Parke-Davis, 1982
Oxford Biomedical Research, 1984-present
Searle and Co., 1985
Health Effects Institute, 1985-1987
Proctor and Gamble, 1987
Searle and Co., 1988
Proteins International, 1987-present
Monsanto, 1993-

Previous Research Support

Wayne State University, "*Faculty Research Award*" Direct Costs: 6/1/76-8/31/76, \$6,000.

American Chemical Society - Petroleum Research Fund, "*The Oxygenation of Polycyclic Aromatic Hydrocarbons by Prostaglandin Synthetase*" Direct Costs: 6/1/76-8/31/79, \$9,000.

American Cancer Society, BC-244 "*The Role of Prostaglandin Synthetase in the Metabolic Activation of Chemical Carcinogens*" 1/1/77-12/31/88, \$625,836.

National Institutes of Health, R01-GM 23642 "*Studies on Prostaglandin Synthase*" Direct Costs: 1/1/77-6/30/90, \$750,000.

National Institutes of Health, R01-CA 22206 "*Studies on Malondialdehyde*" Direct Costs: 8/1/77-4/30/88, \$595,415

Merck and Co., "*Studies on Prostaglandin Synthetase*" Direct Costs, 9/1/77-8/31/78, \$10,000.

Searle and Co. "*Malondialdehyde Levels in Human Cervical Mucous*" Direct Costs: 9/1/81-8/31/83, \$71,000

Miles Institute for Preclinical Pharmacology, "*Metabolism of Nafazatrom*" Direct Costs: 7/1/82-6/30/83, \$30,000.

National Institutes of Health, R01-CA 32506 "*Cancer Chemoprevention and Arachidonate Metabolism*" Direct Costs: 8/1/82-6/30/85, \$106,278.

American Cancer Society, FRA-243 "*Faculty Research Award*" Direct Costs: 9/1/82-9/1/87, \$150,000

National Institutes of Health, R01-CA 43209 "*Peroxyl Radicals, Hydroperoxides, and Carcinogenesis*" Direct Costs: 8/1/86-7/31/88, \$153,998.

Harper Hospital, "*Mechanisms of Metastasis*" Coinvestigator with K. Honn, C. Johnson, and B. Sloane, Direct Costs: 9/1/85-12/31/87, \$575,000.

Thomae Pharmaceuticals, "*Studies on Metastasis*" Direct Costs: 4/1/86-9/30/87, \$60,000.

Wayne State University, IPPRI Program, "*Construction of Protein Conjugates of Difunctional Carbonyl Compound Adducts to Nucleosides for Production of Immunochemical Reagents for Molecular Dosimetry*" Direct Costs: 4/1/87-3/31/88, \$22,000.

Thomae Pharmaceuticals, "*Studies on Metastasis*" Direct Costs: 4/1/87-9/30/88, \$55,000.

Wayne State University, Center for Chemical Toxicology, "*Investigation of Hydroperoxide Formation and Metabolism During Mouse Skin Tumor Promotion*" Direct Costs: 5/1/88-4/30/89, \$29,850.

Ono Pharmaceutical, "*Studies on 12-Lipoxygenase*" Direct Costs: 1/1/88-12/31/92, \$434,000.

Current Research Support:

National Institutes of Health, R35-CA 47479-05 "*Outstanding Investigator Grant - Polyunsaturated Fatty Acid Metabolism and Carcinogenesis*" Direct Costs: 6/15/94-3/31/95, \$493,773; 4/1/95-3/31/01, \$3,899,965

Invited Symposium Lectures:

American Society of Photobiology Workshop on Chemiluminescence and Lipid Peroxidation
Colorado Springs, Colorado (February 22, 1980).
10th Linderstrom-Lang Conference, Skokloster, Sweden (June 20-23, 1980).
Gordon Conference on Drug Metabolism, Plymouth, New Hampshire (July 21-25, 1980).
Gordon Conference on Oxygen Radicals in Biology & Medicine Ventura, California (January 12-16, 1981).
Winter Prostaglandin Meeting, Clearwater, Florida (March 1-5, 1981).
International Symposium on Metabolism and Pharmacokinetics of Environmental Chemicals in Man, Sarasota, Florida (June 8-12, 1981).
National Cancer Institute Workshop on Chemoprevention of Carcinogenesis, Bethesda, Maryland (June 25-26, 1981).
International Conference on Prostaglandins and Cancer, 1981, Washington, D. C. (August 31-September 3, 1981).
Symposium on Nafazatrom, Port Chester, New York (October 1-2, 1981).
V International Conference on Prostaglandins, Florence, Italy (May 18-22, 1982).
Conference on Enzyme Chemistry, Northwestern University Medical School, Evanston, Illinois (June 17, 1983).
Gordon Research Conference on Drug Metabolism, New Hampshire (July 29, 1983).
Workshop on Eicosanoids, University of Michigan, Ann Arbor, Michigan (October 20, 1983).
Symposium on Comparison of Radiation and Chemically-Induced Cancer, National Cancer Institute, Gaithersburg, Maryland (December 6-8, 1983).
Chemoprevention Workshop, National Cancer Institute, Bethesda, Maryland (May 4, 1984).
Mechanisms of Metastasis, Detroit, Michigan (June 2, 1984).
Ninth European Workshop on Drug Metabolism, Pont a Mousson, France (June 13, 1984).
Symposium on Polycyclic Hydrocarbons and Cancer, American Chemical Society, Philadelphia, Pennsylvania (August 29, 1984).
Workshop on the Role of Cyclic Nucleic Acid Adducts in Mutagenesis and Carcinogenesis, Lyon, France (September 18, 1984).
Kyoto Conference on Prostaglandins, Kyoto, Japan (November 27, 1984).
Prostaglandin Biochemistry Workshop, Otsuka Research Institute, Tokushima, Japan (November 29, 1984).
Workshop on Oxygen Radicals and Cancer, Berkeley, California (February 8-9, 1985).
Gordon Conference on Oxy-Radicals in Biology and Medicine, Santa Barbara, California (February 11-15, 1985).
American Association for Cancer Research Symposium on Non-Cytochrome P-450-Mediated Carcinogen Metabolism and Activation, Houston, Texas (May 25, 1985).
Gordon Conference on Free Radicals, Plymouth, New Hampshire, (June 10-14, 1985).
Symposium on Arachidonic Acid Metabolism, American Chemical Society, Chicago, Illinois (September 11, 1985).
Symposium on Health Effects of Automotive Emissions, Dearborn, Michigan (November 1, 1985).
Symposium on Radical-Induced Damage to DNA, Michigan State University, East Lansing, Michigan (November 9, 1985).
US-Japan Cooperative Meeting on Oxygen Radicals and Cancer, Makaha, Hawaii (March 27-28, 1986).
FASEB Symposium on Peroxidase Mechanisms in Chemical Carcinogenesis, St. Louis, Missouri (April 15, 1986).
VI International Conference on Prostaglandins, Florence, Italy (June 3-6, 1986).

FASEB Summer Research Conference on Lung Pharmacology and Pathophysiology, Saxton's River, Vermont (July 27-August 1, 1986).
National Cancer Institute Workshop on Free Radicals and Cancer, Santa Barbara, California (February 8, 1987).
Gordon Conference on Oxy-Radicals in Biology and Medicine, Santa Barbara, California (February 9-13, 1987).
American Cancer Society Workshop on Mechanisms of Tumor Promotion, Key Biscayne, Florida (February 23-25, 1987).
Second International Conference on Anticarcinogenesis and Radioprotection, Gaithersburg, Maryland (February 9-12, 1987).
Winter Prostaglandin Meeting, Orlando, Florida (March 12-14, 1987)
Gordon Conference on Cancer, New London, New Hampshire (August 17-21, 1987)
UCLA Symposium on Oxygen Radicals in Molecular Biology and Pathology, Park City, Utah (January 25-29, 1988)
Society for Free Radical Research International Conference on Medical, Biochemical and Chemical Aspects of Free Radicals, Kyoto, Japan (April 9-13, 1988)
Taipei Conference on Prostaglandin and Leukotriene Research, Taipei, Taiwan, R.O.C. (April 22-24, 1988)
FASEB Symposium on Oxy Radicals and Cytochrome P-450, Las Vegas, Nevada (May 5, 1988)
National Science Foundation Workshop of Physical Organic Chemistry (Reactive Intermediates), Lake Tahoe, California (May 21-23, 1988)
Gordon Conference on Pyrroles, Wolfeboro, New Hampshire (July 25-29, 1988)
ASPET Symposium on Reactions of Hydroperoxides in Biological Systems, Montreal, Quebec (October 11, 1988)
Eleventh Enzyme Mechanisms Conference, St. Petersburg, Florida (January 6-8, 1989)
Winter Prostaglandin Meeting, Keystone, Colorado (January 17-19, 1989)
Symposium on Biological Oxidations, American Chemical Society, Central Regional Meeting, Cleveland, Ohio (May 31-June 2, 1989)
Risk Factors and Mechanisms in Carcinogenesis, Joint Symposium of the Sonderforschungsbereiche 172 and 302, Wurzburg, West Germany (June 26-28, 1989)
Eicosanoids and Bioactive Lipids in Cancer and Radiation Injury, Detroit, Michigan (October 11-14, 1989)
International Symposium on Biological Oxidation Systems, Bangalore, India (October 22-26, 1989)
DeChatelet Conference, Bowman Gray School of Medicine, Winston-Salem, North Carolina (November 29, 1989)
Fourth International Conference on Biological Reactive Intermediates, Tuscon, Arizona (January 14-17, 1990)
FASEB Symposium on Oxygen Radicals in Tissue Injury, Washington, D.C. (April 2, 1990)
VII International Conference on Prostaglandins, Florence, Italy (May 28-June 1, 1990)
VIII International Symposium on Microsomes and Drug Oxidations, Stockholm, Sweden (June 25-29, 1990)
Harden Conference on Free Radicals: Cell Growth, Disease and Repair Mechanisms, Wye, England (September 2-7, 1990)
Fourth Southeastern Regional DNA Symposium, Oxford, Mississippi (October 26-27, 1990)
Twenty First Symposium of the Princess Takamatsu Cancer Research Fund, Tokyo, Japan (November 13-15, 1990)
Symposium on the Role of Oxygen Free Radicals in Tissue Damage, Kansas City, Missouri, (December 3-4, 1990)
Symposium on Generation of Reactive Intermediates, Canadian Federation of Biological Societies, Kingston, Ontario (June 11, 1991)

NIEHS Environmental Health Sciences Centers Directors Meeting, Nashville, Tennessee, (June 17, 1991)
International Symposium on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury, Berlin, Germany (September 18-21, 1991)
Symposium on Peroxidases and Peroxyl Radicals in Toxicity, Society of Toxicology Annual Meeting, Seattle, Washington (February 25, 1992) Also symposium cochairman.
Twenty-Sixth European Symposium on Bioorganic Chemistry, Gregynog, Wales (May 15-19, 1992), Plenary Lecture
Eighth International Conference on Prostaglandins and Related Compounds, Montreal, Canada (July 27-31, 1992) Also session chairman
Eighteenth Symposium on Toxicology and Environmental Health, Japanese Pharmacology Society (October 27, 1992) Plenary Lecturer
Fourth North American Meeting of the International Society for the Study of Xenobiotics Miami, Florida (November 5, 1992)
DNA Adducts of Carcinogenic and Mutagenic Agents. Chemistry, Identification, and Biological Significance Stockholm, Sweden (November 18-21, 1992)
American Association of Cancer Research Special Conference "Chemicals, Mutations, and Cancer," Banff, Canada (December 7-12, 1992)
American Association of Cancer Research Task Force on Chemoprevention Workshop, Philadelphia, Pennsylvania (February 25, 1993)
Fourth International Conference on Anticarcinogenesis and Radiation Protection, Baltimore, Maryland (April 18-23, 1993)
American Chemical Society Workshop on Chemical Mechanisms in Toxicology, Washington, D.C. (August 2-4, 1993)
Third International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury, Washington, D.C. (October 13-16, 1993)
Workshop on Non-Steroidal Antiinflammatory Agents and Cancer American Health Foundation, New York (October 28, 1993)
American Chemical Society Workshop on Chemical Mechanisms in Toxicology, Clearwater, Florida. (November 8-9, 1993)
International Symposium on Molecular Biology of the Arachidonate Cascade, Kyoto, Japan (December 6-7, 1993)
American Association of Cancer Research Meeting on Risk Assessment in Environmental Carcinogenesis, Whistler, British Columbia (January 17-22, 1994)
American Cancer Society Workshop on NSAID's and Colon Cancer Prevention, Atlanta, Georgia (March 21-22, 1994)
Gordon Conference on Mutagenesis, Plymouth, New Hampshire (June 27-July 1, 1994)
International Union of Pharmacology, Montreal (July 25-29, 1994)
Thirteenth Symposium on Molecular Biology - Molecular Mechanisms of Toxicity, Pennsylvania State University (August 3-5, 1994)
Symposium on Radicals in Biochemistry and Chemistry, Durham, North Carolina (September 16-17, 1994)

Invited Lectures:

1976

University of Michigan, Flint, Chemistry
University of Michigan, Dearborn, Chemistry

1977

University of Michigan, Dearborn, Chemistry
Oakland University, Chemistry
University of Detroit, Chemistry
Duke University, Pharmacology
National Institute of Environmental Health Sciences

1978

Cleveland State University, Chemistry
University of Wisconsin, Madison, College of Pharmacy
University of Toledo, Chemistry
Ohio University, Chemistry
Veteran's Administration Geriatric Research Center, St. Louis

1979

Wayne State University, Chemistry
Lawrence Institute of Technology, Chemistry
Ohio Wesleyan University, Chemistry
Michigan State University, Pharmacology and Toxicology
University of Michigan, Dearborn, Natural Sciences

1980

University of Texas Health Sciences Center, Dallas, Biochemistry
University of Detroit, Chemistry
Wayne State University, Biochemistry
St. John Fisher College, Chemistry
Niagara University, Chemistry
University of Rochester, Chemistry
National Institute of Environmental Health Sciences

1981

Ford Motor Company, Dearborn, MI
Mercy College, Chemistry
University of Texas Health Sciences Center, Dallas, Biochemistry
North Texas State University, Chemistry
Wayne State University, Chemistry
Michigan Cancer Foundation
McArdle Laboratory for Cancer Research, University of Wisconsin, Madison
New York Medical College, Pharmacology
Western Michigan University, Chemistry
Hope College, Chemistry
Detroit Physiological Society

1982

Warner-Lambert/Parke-Davis
The Upjohn Company
Hoffmann-LaRoche
Wayne State University, Biology
Wayne State University, Pharmacology
University of Chicago, Chemistry
Bayer Pharmaceuticals, Wuppertal, West Germany
Federal Cancer Research Center, Heidelberg, West Germany
Wayne State University Medical School, Biochemistry
Oakland University
Pfizer Central Research
Massachusetts Institute of Technology, Department of Nutrition and Food Science

1983

University of California, San Francisco, Pharmaceutical Chemistry
University of California, Berkeley, Biochemistry
University of Rochester, Pharmacology
University of Rochester Cancer Center
University of Michigan, School of Public Health
Central Michigan University
University of Toledo, Chemistry
Frederick Cancer Research Institute

1984

National Institute of Environmental Health Sciences
Oakland University, Chemistry
Wayne State University, Chemistry
Northwestern University School of Medicine, Pharmacology
University of Virginia, Chemistry
University of Guelph, Chemistry
Ecole Normale Supérieure, Chemistry, Paris, France
University of Strasbourg, Molecular Biology
University of Michigan School of Public Health
American Cancer Society Workshop, Traverse City Workshop
Vanderbilt University School of Medicine, Biochemistry
University of Detroit, Chemistry
Kochi University School of Medicine, Biochemistry, Kochi, Japan
Keio University School of Medicine, Biochemistry, Tokyo, Japan
University of Philippines School of Medicine, Manila, The Philippines.
University of Philippines, Chemistry, Quezon City, The Philippines.

1985

University of Rochester, Chemistry
Harvard Medical School, Biological Chemistry
Wayne State University, School of Medicine, Physiology

1986

Case Western University, Chemistry
Pennsylvania State University, Biochemistry
Pennsylvania State University, Chemistry
University of Texas System Cancer Center

University of Texas, Austin, Chemistry
Johns Hopkins University, Environmental Health Sciences
Washington State University, Chemistry
University of Toronto, Pathology
University of Minnesota, Chemistry
Wayne State University, Food Science and Nutrition
Medical College of Wisconsin, Biochemistry
University of Alberta Cancer Center
Vanderbilt University, Biochemistry
Vanderbilt University, Center for Molecular Toxicology

1987

Massachusetts Institute of Technology, Applied Biological Sciences
Health Effects Institute
Warner-Lambert/Parke-Davis, Biochemistry Division
Michigan State University, Biochemistry
University of California-Berkeley, Biochemistry
Eppley Institute for Cancer Research
University of Colorado-Boulder, School of Pharmacy
University of California San Francisco, School of Pharmacy
University of Michigan, Biological Chemistry
Duke University, Chemistry
Wayne State University, Pathology
Indiana University, Chemistry
Northeast Regional American Chemical Society Medicinal Chemistry Group
Wayne State University, Biochemistry

1988

University of Utah, Chemistry
Wayne State University, Chemistry
Oakland University, Chemistry
Searle Research and Development
Tokyo University, Pharmaceutical Sciences
National Cancer Center, Tokyo, Biology Division
National Yang Ming Medical College, Taipei, Institute for Biochemistry
University of Guelph, Chemistry
University of Guelph, Nutrition
Michigan Cancer Foundation
Vanderbilt University, Chemistry
Vanderbilt University, Biochemistry

1989

Wayne State University, Pharmacology
University of Toledo, Medicinal Chemistry
Vanderbilt University, Center in Molecular Toxicology
Vanderbilt University, Program in Molecular Biophysics
Bowman Gray School of Medicine, Cancer Center

1990

Vanderbilt University, Molecular Biology
University of Cincinnati, Institute of Environmental Health
M.D. Anderson Cancer Center and Tumor Institute, Cell Biology

University of Texas, College of Pharmacy
University of Pennsylvania, Pharmacology
Vanderbilt University, Pharmacology
Vanderbilt University, Center in Molecular Toxicology
Wellcome Research Laboratories, Division of Pharmacology
Tokushima University, Biochemistry
Ono Pharmaceutical Research Laboratories
Tokyo University, Department of Plant Chemistry and Pharmacognosy
Tokyo Metropolitan Institute of Aging
Upjohn Company, Tsukuba Research Laboratories
Emory University, Biochemistry

1991

Vanderbilt University, Pharmacology
Vanderbilt University, Center in Molecular Toxicology
University of Texas Southwestern Medical School at Dallas, Pharmacology
Vanderbilt University, Biochemistry
American Health Foundation
Cornell University Medical Center, Pharmacology
Schering Pharma, Berlin
American Chemical Society, Lexington Section, Lexington, Kentucky
University of Louisville Medical School, Biochemistry
Vanderbilt University, Center in Molecular Toxicology Open House
Rhodes College, Chemistry
Belmont University, Chemistry
Vanderbilt University, Center in Molecular Toxicology

1992

University of California San Francisco, Pharmaceutical Chemistry
Vanderbilt University, Medicine - Oncology Division
Vanderbilt University, Medicine - Nephrology Division
National Institute of Environmental Health Sciences
Vanderbilt University, Center in Molecular Toxicology
Vanderbilt University, Center in Molecular Toxicology Open House
Tokyo College of Pharmacy, Tokyo
National Institute of Hygienic Sciences, Tokyo
Karolinska Institutet, Stockholm, Medical Chemistry

1993

University of Texas Health Science Center, San Antonio, Biochemistry
Mallinckrodt Medical Products
Vanderbilt University School of Medicine, Pathology
University of Nebraska, Chemistry
Vanderbilt University, Chemistry
Rutgers University, Chemical Biology and Pharmacognosy
Vanderbilt University School of Medicine, Center in Molecular Toxicology
Monsanto
Western Maryland College, Chemistry
Pennsylvania State University, Molecular and Cellular Biology
Vanderbilt University School of Medicine, Medical Oncology
Banyu Pharmaceutical, Tsukuba, Japan
Tokyo University, Center for Advanced Research

Vanderbilt University School of Medicine, Clinical Pharmacology

1994

University of Arizona, Southwest Center for Environmental Health Sciences

Vanderbilt University School of Medicine, Center in Molecular Toxicology

University of Arkansas Medical School, Pharmacology and Toxicology

Institut Gustave-Roussy, Pharmacologie Moleculaire

Universite Rene Descartes, Laboratoire de Chimie et Biochimie

Schering-Plough

PUBLICATIONS

Refereed Journals:

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2. N. A. Porter, L. J. Marnett, C. H. Lochmüller, G. L. Closs, and M. Shobataki, "Application of Chemically-Induced Dynamic Nuclear Polarization to a Study of the Decomposition of Unsymmetric Azo Compounds," *J. Amer. Chem. Soc.*, **94**, 3664-3665 (1972).
3. N. A. Porter and L. J. Marnett, "The Photolysis of Unsymmetric Azo Compounds: *cis*-Azo Compound Intermediates," *J. Amer. Chem. Soc.*, **95**, 4361-4367 (1973).
4. L. J. Marnett, P. Smith, and N. A. Porter, "An EPR Investigation of Hydrazyl Radicals Formed in Azo Compound Photolysis," *Tetrahedron Lett.*, **13**, 1081-1084 (1973).
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7. L. J. Marnett and C. L. Wilcox, "Stimulation of Prostaglandin Biosynthesis by Lipoic Acid," *Biochim. Biophys. Acta*, **487**, 222-239 (1977).
8. L. J. Marnett and M. J. Bienkowski, "Non-Enzymatic Reduction of Prostaglandin H by Lipoic Acid," *Biochemistry*, **16**, 4303-4307 (1977).
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13. L. J. Marnett, M. J. Bienkowski, and W. R. Pagels, "Oxygen-18 Investigation of the Prostaglandin Synthetase-Dependent Cooxidation of Diphenylisobenzofuran," *J. Biol.Chem.*, 254, 5077-5082 (1979).
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